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EXAMINER	
FORD, ALLISON M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 10/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/775,341	TANAKA ET AL.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 27-64* is/are pending in the application.

4a) Of the above claim(s) *9 and 27-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-13* is/are rejected.

7)☒ Claim(s) *4 and 6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments/Amendments

Applicant's arguments filed 6 July 2005, with respect to claims 1-8 and 10-13, have been considered but are moot in view of the new ground(s) of rejection. Amendments to claims 10 and 11 have been entered. Claims 14-26 have been cancelled. Claims 1-13 and 27-64 remain pending in the current application.

Claim Objections

Applicant is advised that should claim 4 be found allowable, claim 6 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. Alternatively, if claim 6 is found allowable, claim 4 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants have amended claim 10 to require the concentration of the calcium chloride in the gel matrix to be 10-40 mM. Applicants point to paragraph 0046 (spanning pages 11-12) of the specification for support for this amendment where lines 3-4 of page 12 state, "the concentration of the transfection reagent in the gel matrix will be higher than in the total reaction volume- on the order of 5 mM to 0.1 M, preferably 10-40 mM." However, the specification teaches the preferred concentration of the transfection reagent, not the concentration of calcium chloride. In calcium phosphate mediated transfection $CaPO_4$-DNA is the transfection reagent, not calcium chloride. In calcium phosphate mediated transfection DNA and calcium chloride are mixed and added to a solution of HEPES-buffered saline (which contains phosphate); upon contact with the HEPES the $CaCl_2$/DNA precipitates $CaPO_4$-DNA, it is this precipitate that is used as the transfection reagent (See Ausubel et al, pages 9.1.1-9.1.2). Therefore, because applicant's specification teaches the concentration of the transfection reagent is preferably 10-40 mM, they are actually requiring the concentration of the $CaPO_4$-DNA to be 10-40 mM, and are silent on the concentration of calcium chloride. Therefore, the concentration of calcium chloride in the gel matrix is considered new matter, as it is not disclosed anywhere in the disclosure as originally filed. The new matter must be cancelled in response to this office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4 and 6-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claims 4 is directed to a multiwell plate for transfecting a eukaryotic cell wherein the bottom of at least some of the wells are at least partially coated with a composition comprising a metal

salt and a matrix complex. Claim 6 is similarly directed to a multiwell plate for transfecting a eukaryotic cell wherein the bottom of at least some of the wells are at least partially coated with a composition comprising a metal salt and the composition is retained on the multiwell plate with a matrix complex.

First, it is not clear what "a matrix complex" means. Particularly, it is not clear how a composition further comprises a matrix complex, as a composition is usually contained within a matrix. In this context a matrix would be interpreted to be a cross-linked substrate, as in a gelatin matrix; however, it is not clear what the qualifier "complex" means.

Second, claims 4 and 6 appear to be substantial duplicates of one another; it appears that for the composition to be retained on the multiwell plate with a matrix complex, the matrix complex must be combined with the metal salt, making them a single composition.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, and 4-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Webb et al (US Patent 6,670,129).

Applicant's claim 1 is directed to a multiwell plate for transfecting a eukaryotic cell wherein the bottom of at least some of the wells are at least partially coated with a composition comprising a metal salt. Claim 2 requires the metal salt to be a calcium salt. Claim 4 requires the composition to further comprise a matrix complex. Claim 5 requires the composition to be retained on the multiwell plate.

Claim 6 requires the composition to be retained on the multiwell plate with a matrix complex. Claim 7 requires the matrix complex to be proteins. Claim 8 requires the proteins to be gelatin.

Webb et al teach a method for performing reverse transfection of eukaryotic cells and a multiwell plate for performing the reverse transfection. Webb et al's method involves printing a mixture of foreign biomolecules, such as DNA, and a transfection agent, such as calcium phosphate, onto the wells of a microplate; Webb et al teach that the biomolecules, such as DNA, can be contained in a solvent, such as gelatin (See col. 6, ln. 46-col. 8, ln 48 (especially col. 8, lines 29-31) & col. 11, ln 53-58). Therefore Webb et al teach a microwell plate wherein at least some of the wells are coated on the bottom with a composition comprising calcium phosphate (a calcium salt) and gelatin (which applicant calls both the composition comprising gelatin (matrix complex) and the composition being retained on the gelatin (matrix complex)) (Claims 1, 2 and 4-8). Therefore the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 and 10-13 are rejected under 35 U.S.C.103(a) as being unpatentable over Webb et al (US Patent 6,670,129), in view of Ausubel et al (Current Protocols in Molecular Biology, 1988).

Applicant's claim 1 is directed to a multiwell plate for transfecting a eukaryotic cell wherein the bottom of at least some of the wells are at least partially coated with a composition comprising a metal salt. Claim 2 requires the metal salt to be a calcium salt. Claim 3 requires the metal salt to be calcium chloride or calcium acetate. Claim 4 requires the composition to further comprise a matrix complex. Claim 5 requires the composition to be retained on the multiwell plate. Claim 6 requires the composition

to be retained on the multiwell plate with a matrix complex. Claim 7 requires the matrix complex to be proteins. Claim 8 requires the proteins to be gelatin.

Applicant's claim 10 is directed to a cell culture/transfection device for transfecting a eukaryotic cell, comprising a solid surface, wherein the solid surface is coated with calcium chloride in a gel matrix, wherein the concentration of the calcium chloride in the gel matrix is 10-40 mM. Claim 11 requires the surface to be selected from the group consisting of flasks, dishes, tubes, multiwell plates, slides and implanted devices. Claim 12 requires the solid surface to be glass, polystyrene or epoxy resins. Claim 13 requires the solid surface to be selected from a slide and a multi-well plate.

Webb et al teach a method for performing reverse transfection of eukaryotic cells and a multiwell plate for performing the reverse transfection. Webb et al's method involves printing a mixture of foreign biomolecules, including DNA, and a transfection agent, such as calcium phosphate, onto the wells of a microwell plate (See col. 6, ln. 46-col. 8, ln 48, especially col. 8, lines 29-31).

Though Webb et al describe calcium phosphate as *the transfection reagent*, it was well known to one of ordinary skill in the art at the time the invention was made that it is actually the $CaPO_4$-DNA complex that functions as the transfection reagent in calcium phosphate mediated transfections (See, e.g., Ausubel et al, 9.1.1).

Therefore, though Webb et al teach mixing the 'transfection reagent' calcium phosphate with the biomolecules (DNA) and printing the mixture (calcium phosphate + DNA) onto the wells of the microwell plate (See col. 7, ln 29-31) it would have been obvious to one of ordinary skill in the art to interpret this to mean the $CaPO_4$-DNA transfection agent can be prepared, by means known in the art, and then the resulting mixture, $CaPO_4$-DNA transfection agent, is coated onto the wells of the microwell plates for reverse transfection. Standard protocol for forming the $CaPO_4$-DNA complex (transfection reagent) involves combining a HEPES-buffered saline solution with a solution containing $CaCl_2$ and

DNA (See Ausubel et al, 9.1.1); thus the mixture comprising the transfection agent comprises calcium chloride (Claims 1-3).

Webb et al also teach that the biomolecules, such as DNA, can be contained in a solvent, such as gelatin (which applicant calls a matrix complex) (See Webb et al, col. 11, ln 53-58). While Webb et al only teach applying the DNA in a gelatin solution to the microwell plates, it would have been obvious to one of ordinary skill in the art to combine the mixed $CaPO_4$-DNA transfection agent with gelatin, and to apply the composition of $CaPO_4$-DNA in a gelatin matrix to the wells of the microwell plate (which applicant calls further including a matrix complex (gelatin) in the composition, as well as retaining the composition on the multiwell plate with a matrix complex (gelatin)) (Claims 4-8). It would have been obvious to one of ordinary skill in the art to combine the $CaPO_4$-DNA complex with gelatin and apply the entire composition to the wells of the microwell plate in order to provide a suitable delivery vehicle for the $CaPO_4$-DNA complex. Gelatin is commonly used in the art to aid in adhesion to substrates such as microwell plates (See, e.g. Webb et al); therefore one of ordinary skill in the art would have been motivated to use gelatin to apply the $CaPO_4$-DNA transfection reagent to the microwell plates in order to carry the $CaPO_4$-DNA complex and to aid in adhesion to the substrate. One would have expected success because gelatin is a well known and commonly used delivery vehicle for transfer of compositions to substrates, and Webb et al teach successfully transferring DNA in a gelatin matrix to the wells of a multiwell plate; therefore one would expect equal success transferring a composition of $CaPO_4$-DNA in a gelatin matrix to the same multiwell plates.

Regarding the concentration of calcium chloride in the gel matrix, it appears that this concentration is dependent on the initial quantity of calcium chloride used to form the $CaPO_4$-DNA transfection reagent. Ausubel et al teach that concentration of DNA is a result effective variable, and can vary from 10-50 ug per 10-cm dish (See Ausubel et al, pg 9.1.1); therefore, because the concentration of

calcium chloride depends on the concentration of DNA used, the concentration of calcium chloride is also a result effective variable that would be routinely optimized by one of ordinary skill in the art (Claim 10).

Though the example provided Webb et al (Pg. 19) uses a microwell plate, they also teach that the transfections can be performed on culture dishes and any other suitable substrate geometries. Therefore, though Webb et al do not specifically state flasks, tubes, slides or implanted devices, it would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the transfection on any solid surface, including flasks, tubes and/or implanted devices (See Webb et al, col. 6, ln 46-63) (Claims 11 and 13). One of ordinary skill in the art would have been motivated to use any solid surface, including flasks, dishes, tubes, multi-well plates, slides, and/or implanted devices based on their personal preference and experimental design, as all are functional equivalents of one another for the present purpose. One of ordinary skill in the art would be motivated to use flasks or dishes, such as culture flasks or culture dishes, or multi-well plates because they can easily hold cell culture solution; multi-well plates would especially be useful when multiple samples of different cells are to be transfected, in order to provide separate wells for each cell type. One of ordinary skill in the art would have been motivated to use an implantable device in order to transfect cells prior to transplanting them to a patient, for example, an artificial dermis matrix that is to be used to transfect cells with growth factors to increase the survive rate of the transplanted cells. One would have expected success using any geometric surface because Webb et al teach that any solid geometric surface, suitable for the individual needs is acceptable.

Finally, Webb et al teach suitable substrates can be comprised of, or coated, with glass or polystyrene (See Webb et al, col. 7, ln 66-col. 8, ln 7 & col. 8, ln 33-50) (Claim 12). Additionally, though they do not specifically list epoxy resins as a material, it would have been obvious to one of ordinary skill in the art to use epoxy resins as at least part of the solid surface (Claim 12). One of ordinary skill in the art would have been motivated to use cured epoxy resin plastics based on availability of materials, for example, if epoxy resin slides or dishes, or glass-reinforced plastics, that comprise epoxy, were readily

available. One would have had a reasonable expectation of success using any glass, plastic, or epoxy resin material that is suitable grade for cell culture based on Webb et al's teachings that any suitable solid material can be used.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651

LEON B. LANKFORD, JR.
PRIMARY EXAMINER